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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/488,442	01/20/2000	James E. Darnell JR.	600-1-195B	4454

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EXAMINER
GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/488,442	Applicant(s) DARNELL ET AL.	
	Examiner Jeanine A Goldberg	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,97-113 and 115-119* is/are pending in the application.

4a) Of the above claim(s) *98-107* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,97,108-113 and 115-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed October 8, 2002. Currently, claims 97-113, 115-119 are pending. Claims 98-107 have been withdrawn as drawn to non-elected subject matter.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

3. Any objections and rejections not reiterated below are hereby withdrawn in view of applicant's arguments and the amendments made to the claims.

Maintained Rejections

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1, 97, 108-113, 115-119 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The claims are drawn to Stat 3 proteins, immunogenic fragments, and fusion proteins.

The specification teaches that receptor recognition factors have been characterized that appear to interact directly with receptors that have been occupied by their ligand on cellular surfaces, and which in turn either become active transcription factors, or activate or directly associate with transcription facts that enter the cells nucleus and specifically binds on predetermined sites and thereby activates the gene. The specification teaches receptor recognition factors have been termed signal transducers and activators of transcription, STAT. The specification teaches that the exact structure of each receptor recognition factor will understandably vary so as to achieve this ligand and activity specificity (page 10). The specification teaches the cloning of the 19sf6 gene and deduced amino acid (Stat3, SEQ ID NO: 12). Stat3 has been found to be activated as a DNA binding protein through posphorylation on tyrosine in cells treated with EGF or IL-6, but not after IFN-gamma treatment (page 70). Stat3 was present in cells as Seen in Table (page 72).

The specification teaches the general utility for Stat3 is for the promise of a broad spectrum of diagnostic and therapeutic utilities (page 11, lines 1-5). The specification also generally teaches that an assay system for screening of potential drugs effective to modulate transcriptional activity of target mammalian cells by interrupting or potentiating the recognition factor or factors (page 11, lines 15-20). The diagnostic utility of the present invention extends to the use of the receptor recognition factors in assays to screen for tyrosine kinase inhibitors (page 12, lines 30-31). The present invention also teaches the development of antibodies against the receptor recognition factors (page

13). The therapeutic method could include the method for the treatment of various pathologies or other cellular dysfunctions and derangements by the administration of pharmaceutical compositions that may comprise effective inhibitors or enhancers of activation of the recognition factor or its subunits (page 15).

The specification does not teach a specific utility of the polypeptides, i.e. SEQ ID NO: 12, whereby the invention would be a useful tool for a specific purpose i.e. detection of itself in a sample detects the presence of a specific disease.

The specification asserts that treatment of various pathologies or other cellular dysfunctions and derangements by the administration of pharmaceutical compositions that may comprise effective inhibitors or enhancers of activation of the recognition factor or its subunits. However, the specification does not teach the disease which is associated with the receptor. The specification does not teach the therapy or demonstrate therapeutic results.

The specification has provided no "real world" use for the polypeptide of SEQ ID NO: 12, or fragments thereof that would constitute a substantial utility. Therefore, the specification does not teach a specific or substantial utility for the invention such that the invention would be useful to detect or treat a specific disease state.

It is noted that in the response filed June 19, 2001, applicants have asserted that the receptor recognition factors are involved in signal transduction and play important biological roles (page 5). Further, the response states that "it is now known that the claimed receptor recognition factors are a family of proteins that comprise only seven

members and that are activated by virtually every cytokine and growth factor" (page 6). Applicant's utility however would be required at the time of filing. Similarly, applicant's state that "Stat3 has been implicated in cardiac remodeling, in the clonal stem cell disorder known as polycythemia vera, and protect against apoptosis". Each of these assert utilities are not supported in the instant specification. They appear to have been discovered post filing, namely in 2000 and 2001.

Response to Arguments

The response traverses the rejection. The response asserts that the Stat3 proteins and immunogenic fragments and fusion proteins thereof, are encoded by DNA molecules claimed in US Pat. 6,124,118 and 6,030,808. The response asserts that the "Examiner's position that Stat3 lacks utility is inconsistent with the self-evident utility found for the encoding DNAs". This argument has been reviewed but is not convincing because the nucleic acid and the proteins are patentably distinct groups which were restricted. Moreover, it is noted that each application is examined on its own merits to determine whether the claims are patentable. Thus, based upon the specification, the art and the arguments, the claimed proteins do not appear to meet the utility requirement as set forth in the Utility Guidelines. The response has not demonstrated how the claimed proteins have a utility based upon a utility established for the proteins. The nucleic acid may be found to a have a utility which does not confer a utility on the proteins.

The response also asserts that "Stat3 was found to be activated as a DNA binding protein through phosphoylation on tyrosine in cells treated with EGF." The response asserts that the specification would lead one of skill in the art to recognize the use of Stat3 in modulating the EGF pathway. The response cites several references to support their position. It is noted that none of these references appear to be of record in the instant application, nor in the related applications. Thus, the examiner has not considered these references. In the event that applicant wishes to have these references fully considered, the references may be submitted on a 1449 IDS for consideration.

The response asserts based upon the knowledge in the art at the time the invention was made and the teachings in the specification, one of skill in the art would provide a method for modulating the negative effect of EGF. This argument has been thoroughly reviewed, but found not persuasive because the art nor the specification demonstrate how the Stat3 is involved in the EGF pathway. Furthermore, even if the EGF pathway was modified with Stat3, it is unclear how one could modify the pathway and what effects would be obtained. Based solely on the characterization of the references provided in the response filed October 8, 2002, there is a EGF receptor gene which may be altered in glioma biopsies and overexpressed in cancer. The information relating to a distinct nucleic acid, does not appear to provide a specific and substantial utility for Stat3 protein.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 97, 108-113, 115-119 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The skilled artisan would not know how to make and use the claimed polypeptides at the time the invention was made. It would be undue experimentation for the skilled artisan to determine the diagnostic or therapeutic use.

Additionally, Claims 111-113 are directed to an immunogenic fragment of Stat3 having the amino acid sequence of SEQ ID NO: 12. The specification does not provide any description of immunogenic fragments. The specification does not provide any guidance as to which regions of SEQ ID NO: 12 would be immunogenic fragments. The skilled artisan would be required to perform undue experimentation to determine what regions are essential and therefore, would trigger an immune response. The specification does not appear to provide any definition to immunogenic fragment.

Moreover, the skilled artisan would not know how to make and use polypeptides which minimally contain any 40 amino acids of SEQ ID NO: 12 embedded within a larger sequence.

Response to Arguments

The response traverses the rejection. The response asserts that the claims have a utility and therefore meet the enablement requirements. This argument has been reviewed but is not convincing for the reasons provided in the response to arguments directed to the 101 rejection.

The response asserts, with respect to an immunogenic fragment of SEQ ID NO: 12, that the "description of the antisera obtained with amino acids 688 to 727 of Stat3 clearly refutes the Examiner's stated position as to which regions of SEQ ID NO: 12 would be immunogenic fragments." This argument has been reviewed but is not convincing because the specification may have established a single 42 amino acid region which has some immunogenic activity, however, SEQ ID NO: 12 is 770 amino acids in length. The specification does not provide which fragments from this entire protein is immunogenic.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 111-113 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification teaches describes SEQ ID NO: 12 and the nucleic acid of SEQ ID NO: 11.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its ennoblement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...' required a precise

definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure.

In the instant case, the description in the specification as filed is not sufficient to convey that the applicant was, as of the filing date, in possession of the invention in a manner commensurate in scope with the claims. There is disclosed only a limited number of species, and applicants attempt to claim, on the basis of that single species, any immunogenic fragment of SEQ ID NO: 12. The scope of the claims would appear to be much broader than the particularly disclose species, and one is unable to envision, and the specification does not adequately describe, a commensurate number of species.

With the exception of the SEQ ID NO: 12 referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of protein isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Fevel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Claims 111-113 are directed to an immunogenic fragment of Stat3 having the amino acid sequence of SEQ ID NO: 12. The specification does not provide any description of immunogenic fragments whereby the fragments are smaller than SEQ ID NO: 12.

Therefore, only SEQ ID NO: 12 but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph.

Response to Arguments

The response traverses the rejection. The response asserts that Claims 111-113 are described because they provide both a function (immunogenicity) and sequence (requirement). This argument has been reviewed but is not convincing because the specification has not described which fragments from SEQ ID NO: 12 are immunogenic. The specification describes the entire genus of fragments of SEQ ID NO: 12, however does not describe which of these fragments have immunogenicity properties. The description of a single immunogenic fragment is not adequate description for the genus of immunogenic fragments from SEQ ID NO: 12. Thus for the reasons above and those already of record, the rejection is maintained.

Conclusion

7. No claims allowable.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of formal matters can be directed to the patent analyst, Chantae Dessau, whose telephone number is (703) 605-1237.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jeanine Goldberg
December 22, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600